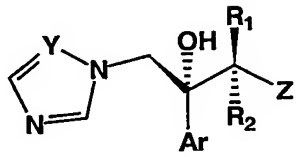
We Claim:

1. A compound having the structure of Formula I



Formula I

and its pharmaceutically acceptable salts, enantiomers, diastereomers, N-oxides, prodrugs, metabolites, polymorphs or pharmaceutically acceptable solvates,

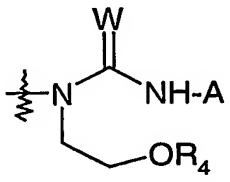
wherein

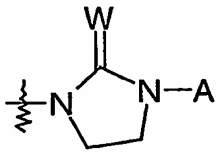
Ar is a five to seven membered heterocyclic ring containing one to four heteroatoms selected from the group consisting of oxygen , nitrogen and sulphur ; phenyl or a substituted phenyl having one to three substituents independently selected from halogen (e.g. chlorine, fluorine, bromine or iodine), nitro, cyano, lower(C_{1-4})alkyl, lower(C_{1-4}) alkoxy, perhalo lower(C_{1-4})alkyl or perhalo lower(C_{1-4})alkoxy;

R_1 and R_2 are independently selected from the group consisting of hydrogen, straight chain or branched alkyl groups having 1 to 3 carbon atoms including methyl, ethyl, propyl;

Y is CH or N;

Z is selected from the group consisting of





wherein

W is selected from O, S, CH-NO_2 and N-CN;

A is hydrogen, unsubstituted or substituted lower (C_{1-10})alkyl, the said substituents being halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4}) perhaloalkoxy, unsubstituted or substituted C_6-C_{10}

aromatic or non aromatic rings with or without one to four heteroatoms independently selected from the group consisting of oxygen, nitrogen and sulphur, the said substituents independently selected from one or more groups including halogen (e.g. fluorine, chlorine, bromine or iodine),nitro, cyano, hydroxy, lower (C_{1-4})alkyl, lower (C_{1-4}) alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4})perhaloalkoxy, BR_3, substituted or unsubstituted five or six membered heterocyclylic ring systems containing one to four heteroatoms are selected from the group consisting of oxygen, nitrogen and sulphur, said heterocyclylic substituents being (C_1-C_8) alkanoyl, lower (C_1-C_4) alkyl, lower (C_1-C_4) alkoxy carbonyl, N lower (C_1-C_4)alkylaminocarbonyl, N,N-dilower(C_1-C_4) alkylaminocarbonyl, N-lower (C_1-C_4) alkylaminothiocarbonyl, N,N-di(lower alkyl) (C_1-C_4) aminothiocarbonyl, N-lower (C_1-C_4) alkyl sulphonyl, phenyl substituted lower (C_1-C_4) alkyl sulphonyl, N-lower (C_1-C_4) alkyl amino, N,N-di(lower alkyl)(C_1-C_4) amino, unsubstituted or substituted phenyl, the said substituents being halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4}) alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4}) perhaloalkoxy, nitro, cyano, amino, $N(R_4)_2$, 5-6 membered heterocyclic rings the preferred heterocycles being 1,3- imidazolyl ,1,2,4 triazolyl and -CHR_5R_6 wherein

R_3 is five or six membered aromatic or non aromatic rings with or without heteroatoms (including oxygen, nitrogen and sulphur);

B is independently selected from $(CH_2)_m$, -S, -$O(CH_2)_m$ and -$S(CH_2)_m$;

m is an integer from 1 to 4;

R_4 is hydrogen, unsubstituted or substituted lower (C_{1-4})alkyl;

R_5 is –$COOR_4$;

R_6 is independently selected from the group consisting of hydrogen, straight chain or branched alkyl with or without substituents, the said substituents being halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkyl ,lower (C_{1-4})alkoxy, lower (C_{1-4})perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4; phenyl or phenyl substituted with halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkoxy, lower (C_{1-4})perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4, heterocyclic rings or substituted heterocyclic rings including imidazole and indole with heteroatoms selected from oxygen, nitrogen and sulphur, substituents on heterocyclic rings are independently selected from halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkyl, lower (C_{1-4})alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4; phenyl or phenyl substituted with halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4.

The compound of claim 1 wherein Ar is thienyl, pyridyl, or halogen substituted phenyl.

The compound of Claim 2 wherein Ar is 2,4-difluorophenyl.

The compound of Claim 1 wherein R_1 and R_2 are independently selected from hydrogen, methyl and ethyl.

The compound of Claim 1 wherein R_1 and R_2 are methyl and hydrogen, respectively.

A compound selected from the group consisting of:

1-[(1R,2R)-2-(2,4-Difluorophenyl)-2-hydroxy-1-methyl-3-(1H-1,2,4-triazol-1-yl)propyl]-1-(2-hydroxyethyl)-3-[4-(1*H*-1-tetrazolyl)phenyl]thiourea.

1-[(1R,2R)-2-(2,4-Difluorophenyl)-2-hydroxy-1-methyl-3-(1H-1,2,4-triazol-1-yl)propyl]-1-(2-hydroxyethyl)-3-[4-(2*H*-2-tetrazolyl)phenyl]thiourea.

1-[(1R,2R)-2-(2,4-Difluorophenyl)-2-hydroxy-1-methyl-3-(1H-1,2,4-triazol-1-yl)propyl]-1-(2-hydroxyethyl)-3-[4-(2,2,3,3-tetrafluoropropoxy)phenyl]thiourea.

1-[(1R,2R)-2-(2,4-Difluorophenyl)-2-hydroxy-1-methyl-3-(1H-1,2,4-triazol-1-yl)propyl]-3-[4-(1*H*-1-tetrazolyl)phenyl]- 2-(1H, 3H)-thioimidazolone.

1-[(1R,2R)-2-(2,4-Difluorophenyl)-2-hydroxy-1-methyl-3-(1H-1,2,4-triazol-1-yl)propyl]-3-[4-(2*H*-2-tetrazolyl)phenyl]- 2-thioimidazolone.

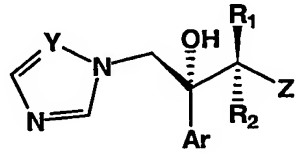
1-[(1R,2R)-2-(2,4-Difluorophenyl)-2-hydroxy-1-methyl-3-(1H-1,2,4-triazol-1-yl)propyl]-3-[4-(2,2,3,3-tetrafluoropropoxy)phenyl]- 2-(1H, 3H)-thioimidazolone.

1-[(1R,2R)-2-(2,4-Difluorophenyl)-2-hydroxy-1-methyl-3-(1H-1,2,4-triazol-1-yl)propyl]-3-[4-cyanophenyl]-2-(1H,3H)-thioimidazolone.

1-[(1R,2R)-2-(2,4-Difluorophenyl)-2-hydroxy-1-methyl-3-(1H-1,2,4-triazol-1-yl)propyl]-3-[5-(2-chloropyridyl)]-2-(1H,3H)-thioimidazolone.

A pharmaceutical composition comprising the compound as defined in claims 1 or 6 and a pharmaceutically acceptable carrier or diluent .

A method of treating or preventing fungal infection in a mammal comprising administering to said mammal a therapeutically effective amount of a compound having the structure of Formula I



Formula I

and its pharmaceutically acceptable salts, enantiomers, diastereomers, N-oxides, prodrugs, metabolites, polymorphs or pharmaceutically acceptable solvates,

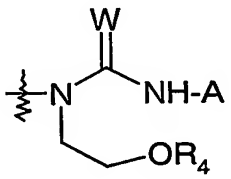
wherein

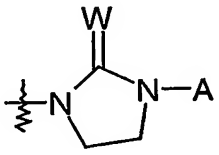
Ar is a five to seven membered heterocyclic ring containing one to four heteroatoms selected from the group consisting of oxygen , nitrogen and sulphur ; phenyl or a substituted phenyl having one to three substituents independently selected from halogen (e.g. chlorine, fluorine, bromine or iodine), nitro, cyano, lower(C_{1-4})alkyl, lower(C_{1-4}) alkoxy, perhalo lower(C_{1-4})alkyl or perhalo lower(C_{1-4})alkoxy;

R_1 and R_2 are independently selected from the group consisting of hydrogen, straight chain or branched alkyl groups having 1 to 3 carbon atoms including methyl, ethyl, propyl;

Y is CH or N;

Z is selected from the group consisting of





wherein

W is selected from O, S, CH-NO_2 and N-CN;

A is hydrogen, unsubstituted or substituted lower (C_{1-10})alkyl, the said substituents being halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4}) alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4}) perhaloalkoxy, unsubstituted or substituted C_6-C_{10} aromatic or non aromatic rings with or without one to four heteroatoms independently selected from the group consisting of oxygen, nitrogen and sulphur, the said substituents independently selected from one or more groups including halogen (e.g. fluorine, chlorine, bromine or iodine),nitro, cyano, hydroxy, lower (C_{1-4})alkyl, lower (C_{1-4}) alkoxy, lower (C_{1-4}) perhaloalkyl, lower(C_{1-4}) perhaloalkoxy, BR_3, substituted or unsubstituted five or six membered heterocyclylic ring systems containing one to four heteroatoms are selected from the group consisting of oxygen, nitrogen and sulphur, said heterocyclylic substituents being (C_1-C_8) alkanoyl, lower (C_1-C_4) alkyl, lower (C_1-C_4) alkoxy carbonyl, N lower (C_1-C_4)

alkylaminocarbonyl, N,N-dilower(C_1-C_4) alkylaminocarbonyl, N-lower (C_1-C_4) alkylaminothiocarbonyl, N,N-di(lower alkyl)(C_1-C_4) aminothiocarbonyl, N-lower (C_1-C_4) alkyl sulphonyl, phenyl substituted lower (C_1-C_4) alkyl sulphonyl, N-lower (C_1-C_4) alkyl amino, N,N-di(lower alkyl)(C_1-C_4) amino, unsubstituted or substituted phenyl, the said substituents being halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4}) alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4}) perhaloalkoxy, niro, cyano, amino, $N(R_4)_2$, 5-6 membered heterocyclic rings the preferred heterocycles being 1,3- imidazolyl ,1,2,4 triazolyl and $-CHR_5R_6$ wherein

R_3 is five or six membered aromatic or non aromatic rings with or without heteroatoms (including oxygen, nitrogen and sulphur);

B is independently selected from $(CH_2)_m$, -S, $-O(CH_2)_m$ and $-S(CH_2)_m$;

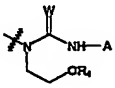
m is an integer from 1 to 4;

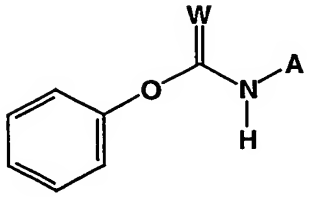
R_4 is hydrogen, unsubstituted or substituted lower (C_{1-4})alkyl;

R_5 is $-COOR_4$;

R_6 is independently selected from hydrogen, straight chain or branched alkyl with or without substituents, the said substituents being halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4}) alkyl, lower (C_{1-4}) alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4; phenyl or phenyl substituted with halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkoxy, lower (C_{1-4})perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4, heterocyclic rings or substituted heterocyclic rings including imidazole and indole with heteroatoms selected from oxygen, nitrogen and sulphur, substituents on heterocyclic rings are independently selected from halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkyl ,lower (C_{1-4})alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4; phenyl or phenyl substituted with halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4}) perhaloalkoxy, SR_4.

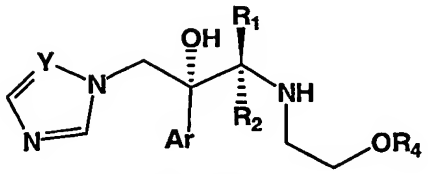
9. A method of treating or preventing a fungal infection in a mammal comprising the step of administering to said mammal a therapeutically effective amount of the pharmaceutical composition according to Claim 7.

10. A process for preparing a compound of Formula II (Formula I, when Z= )



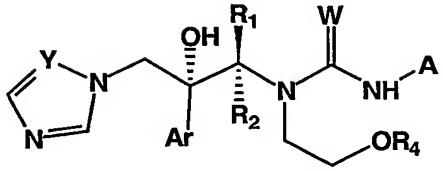
Formula IV

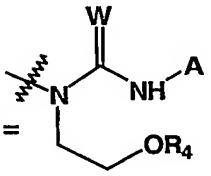
+



Formula V

TEA
EtOAc



Formula II (Formula I, when Z= )

and its pharmaceutically acceptable salts, enantiomers, diastereomers, N-oxides, prodrugs, metabolites, polymorphs or pharmaceutically acceptable solvates,

wherein

Ar is a five to seven membered heterocyclic ring containing one to four heteroatoms selected from the group consisting of oxygen , nitrogen and sulphur ; phenyl or a substituted phenyl having one to three substituents independently selected from halogen (e.g. chlorine, fluorine, bromine or iodine), nitro, cyano, lower(C_{1-4})alkyl, lower(C_{1-4}) alkoxy, perhalo lower(C_{1-4})alkyl or perhalo lower(C_{1-4})alkoxy;

R_1 and R_2 are independently selected from the group consisting of hydrogen, straight chain or branched alkyl groups having 1 to 3 carbon atoms including methyl, ethyl, propyl;

Y is CH or N;

W is selected from O, S, CH-NO_2 and N-CN;

A is hydrogen, unsubstituted or substituted lower (C_{1-10})alkyl, the said substituents being halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4}) alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4}) perhaloalkoxy, unsubstituted or substituted C_6-C_{10} aromatic or non aromatic rings with or without one to four heteroatoms independently selected from the group consisting of oxygen, nitrogen and sulphur, the said substituents independently selected from one or more groups including halogen (e.g. fluorine, chlorine, bromine or iodine),nitro, cyano, hydroxy, lower (C_{1-4})alkyl, lower (C_{1-4}) alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4}) perhaloalkoxy, BR_3, substituted or unsubstituted five or six membered heterocyclylic ring systems containing one to four heteroatoms are selected from the group consisting of oxygen, nitrogen and sulphur, said heterocyclylic substituents being (C_1-C_8) alkanoyl, lower (C_1-C_4) alkyl, lower (C_1-C_4) alkoxy carbonyl, N lower (C_1-C_4) alkylaminocarbonyl, N,N-dilower(C_1-C_4) alkylaminocarbonyl, N-lower (C_1-C_4) alkylaminothiocarbonyl, N,N-di(lower alkyl)(C_1-C_4) aminothiocarbonyl, N-lower (C_1-C_4) alkyl sulphonyl, phenyl substituted lower (C_1-C_4) alkyl sulphonyl, N-lower (C_1-C_4) alkyl amino, N,N-di(lower alkyl)(C_1-C_4) amino, unsubstituted or substituted phenyl, the said substituents being halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4}) alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4}) perhaloalkoxy, nitro, cyano, amino, $N(R_4)_2$, 5-6 membered heterocyclic rings the preferred heterocycles being 1,3- imidazolyl ,1,2,4 triazolyl and -CHR_5R_6 wherein

R_3 is five or six membered aromatic or non aromatic rings with or without heteroatoms (including oxygen, nitrogen and sulphur);

B is independently selected from $(CH_2)_m$, -S, -$O(CH_2)_m$ and -$S(CH_2)_m$;

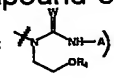
m is an integer from 1 to 4;

R_4 is hydrogen, unsubstituted or substituted lower (C_{1-4})alkyl;

R_5 is –$COOR_4$;

R_6 is independently selected from hydrogen, straight chain or branched alkyl with or without substituents, the said substituents being halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkyl, lower (C_{1-4})alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4; phenyl or phenyl substituted with halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkoxy, lower

(C_{1-4})perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4, heterocyclic rings or substituted heterocyclic rings including imidazole and indole with heteroatoms selected from oxygen, nitrogen and sulphur, substituents on heterocyclic rings are independently selected from halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkyl ,lower (C_{1-4})alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4; phenyl or phenyl substituted with halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4}) perhaloalkoxy, SR_4;

which comprises condensation of the compound of Formula IV with a compound of Formula V, to give the desired compound of Formula II (Formula I, when Z = ).

11. The process of Claim 10 wherein Ar is thienyl, pyridyl, or halogen substituted phenyl.

12. The process of Claim 11 wherein Ar is 2,4-difluorophenyl.

13. The process of Claim 10 wherein R_1 and R_2 are independently selected from hydrogen, methyl and ethyl.

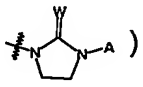
14. The process of Claim 10 wherein R_1 and R_2 are methyl and hydrogen, respectively.

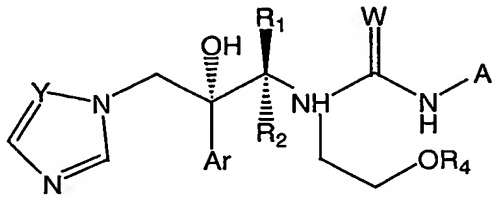
15. The process of Claim 10 wherein the condensation of compound of Formula IV with a compound of Formula V is carried out in a suitable solvent selected from the group consisting of ethyl acetate and N,N-dimethylformamide.

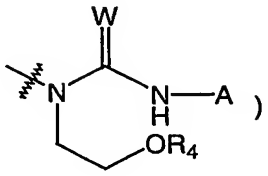
16. The process of Claim 10 wherein the condensation of compound of Formula IV with a compound of Formula V is carried out in the presence of a suitable base.

17. The process of Claim 16 wherein the suitable base is selected from the group consisting of triethylamine, diisopropylamine and pyridine.

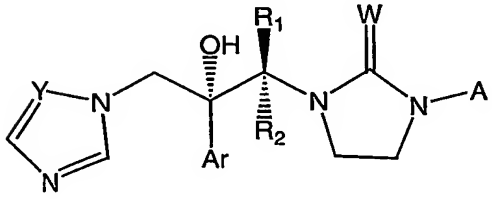
18. The process of Claim 10 wherein the reaction is carried out at a temperature ranging from about 50-150°C.

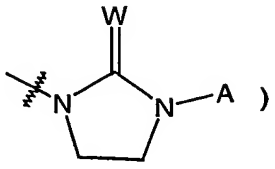
19. A process for preparing a compound of Formula III (Formula I, when Z= )



Formula II (Formula I, when Z = )

TPP, DIAD
DMF



Formula III (Formula I, when Z = )

and its pharmaceutically acceptable salts, enantiomers, diastereomers, N-oxides, prodrugs, metabolites, polymorphs or pharmaceutically acceptable solvates thereof, wherein

Ar is a five to seven membered heterocyclic ring containing one to four heteroatoms selected from the group consisting of oxygen , nitrogen and sulphur ; phenyl or a substituted phenyl having one to three substituents independently selected from halogen (e.g. chlorine, fluorine, bromine or iodine), nitro, cyano, lower(C_{1-4})alkyl, lower(C_{1-4}) alkoxy, perhalo lower(C_{1-4})alkyl or perhalo lower(C_{1-4})alkoxy;

R_1 and R_2 are independently selected from the group consisting of hydrogen, straight chain or branched alkyl groups having 1 to 3 carbon atoms including methyl, ethyl, propyl;

Y is CH or N;

W is selected from O, S, CH-NO_2 and N-CN;

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R_3 is five or six membered aromatic or non aromatic rings with or without heteroatoms (including oxygen, nitrogen and sulphur);

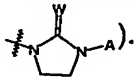
B is independently selected from $(CH_2)_m$, -S, -$O(CH_2)_m$ and -$S(CH_2)_m$;

m is an integer from 1 to 4;

R_4 is hydrogen, unsubstituted or substituted lower (C_{1-4})alkyl;

R_5 is –$COOR_4$;

R_6 is independently selected from hydrogen, straight chain or branched alkyl with or without substituents, the said substituents being halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkyl, lower (C_{1-4})alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4; phenyl or phenyl substituted with halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkoxy, lower (C_{1-4})perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4, heterocyclic rings or substituted heterocyclic rings including imidazole and indole with heteroatoms selected from oxygen, nitrogen and sulphur, substituents on heterocyclic rings are independently selected from halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkyl ,lower (C_{1-4})alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4})perhaloalkoxy, SR_4; phenyl or phenyl substituted with halogen (e.g. fluorine, chlorine, bromine or iodine), hydroxy, lower (C_{1-4})alkoxy, lower (C_{1-4}) perhaloalkyl, lower (C_{1-4}) perhaloalkoxy, SR_4;

which comprises reacting the compound of Formula II under Mitsunobu reaction to give the compound of Formula III (Formula I, when Z= ).

20. The process of Claim 19 wherein the Mitsunobu reaction is carried out with triphenyl phosphine and diisopropyl azodicarboxylate (DIAD)/diethyl azodicarboxylate (DEAD).